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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/402,614 | 03/01/2000 | GAIL PETUNA RISBRIDGER | 229752000800 | 6186 |

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| EXAMINER | |
|---|---|
| YAO, LEI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/402,614 | RISBRIDGER ET AL. | |
| | Examiner | Art Unit | |
| | Lei Yao, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26,40-58,60-63,69,72-93,95,96,98 and 99* is/are pending in the application.

4a) Of the above claim(s) *1-26,40-57,61 and 92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58,60,62,63,69,72-91,93,95,96,98 and 99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***RESPONSE TO ARGUMENTS***

The Amendment filed on 7/20/06 in response to the previous Non-Final Office Action (1/20/06) is acknowledged and has been entered.

Claims 1-26, 40-58, 60-63, 69, 72-93, 95-96, and 98-99 are pending. Claims 1-26, 40-57, 61 and 92 have been withdrawn previously for non-elected invention. Claims 58, 60, 62-63, 69, 72-91, 93, 95-96, and 98-99 are currenly under consideration.

**The text of those sections of Title 35, U.S.Code not included in this action can be found in the prior Office Action.**

***Rejection under 35 USC § 112 1st paragraph***

*Drawn to enablement*

Claims 58, 60, 62-63, 69, 72-91, 93, 95-96, and 98-99 **remain rejected** under 35 U.S.C. 112 first paragraph, as failing to comply with the enablement requirement for the reasons of record in the prior Office Action dated 1/20/06 and state again below:

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are broadly drawn to a method of screening a mammal comprising screening for the down regulation of "inhibin protein levels" wherein the down regulation of the inhibin protein levels relative to the inhibin protein levels of a normal mammal is indicative of the mammal having developed **prostate cancer** (Claim 58). The claimed method is further defined as a method of screening a mammal (or a method of screening a human- Claim 95) for prostate cancer comprising obtaining a biological sample and determining a level of an inhibin protein in said biological sample, and comparing said level determined with a level known to be indicative of a normal mammal, wherein a down-regulation of said inhibin protein level in the biological sample relative to the inhibin protein level of a normal mammal is indicative of the mammal having developed prostate cancer (Claim 83).

The specification teaches (page 43) the down-regulation or complete absence of inhibin subunit protein levels (αN and αC) in a small sampling (12 patients) of human prostate cancer tissues compared to the presence of αN and αC inhibin subunits in adjacent non-malignant regions of the prostate. Similarly, the specification teaches that in situ hybridization was performed using tissue from 8 patients with histological grade 4/5 prostate cancer and confirmed the pattern of protein inhibin localization. Hence, α-subunit gene expression was detected in basal cells in 7 of 8 patients in non-malignant regions and in both basal and secretory cells in some patients while malignant tumor cells in adjacent regions of the same patient biopsies did not display any α-subunit gene expression.

However, upon later re-evaluation co-inventor Risbridger (Risbridger *et al.* "Re-evaulation of inhibin α subunit as a tumour suppressor in prostate cancer". Molecular & Cellular Endocrinology, 2004, Vol. 225, pages 73-76) teach that an expanded study (approximately 174 prostate cancer specimens) of inhibin α subunit protein

expression in prostate cancer revealed the opposite (abstract). That is, unexpectedly, in the majority of cases (89%) there was **more**, rather than less, intense staining of inhibin α subunit in cancer compared to the non-malignant tissue (page 75, 1st column). In their own words, the authors state (page 75, 1st column, 2nd full para.) "The results of the study were unexpected and did not support the previous evidence that inhibin α subunit was down regulated in men with prostate cancer."

Given the evidence set forth in the immediately preceding paragraph, it appears that one of ordinary skill in the art would not be able to successfully detect and or screen prostate cancer by detecting a down-regulation or absence of inhibin protein levels. Thus, it would require undue experimentation to practice the invention as claimed.

The response filed 7/10/06 has been carefully considered but is deemed not to be persuasive. The response discuss a "paradox" of expressing α inhibin in the article cited by the examiner above and states that inhibin is extremely pleiotropic and does exhibit more than one type of activities (page 3, para 2-3). Based on the article, the response states that the tumor suppression activity of inhibin is required in order to prevent the transition of prostate tissue from a non-malignant to a malignant state, where inhbin levels become decreased, this transition occurs and prostate cancer develops and further states that as prostate cancer progresses from a low grade state to a more advanced state, there can occur a switch in function and expression of the inhibin molecule (page 3, para 3). The response further states that the claimed invention is consistent with theory of the article (page 4, para3). In response to this argument, applicants are claiming a method of screening for down regulation of inhibin protein level to indicative of the mammal having developed prostate cancer. First, the claims neither indicate what stage of "developed prostate cancer" is, nor mention that the tumor tissues collected in the given examples of the application are all at the transition stage of the prostate cancer. Second, the applicants disclose examples, in which the biopsies samples are from the patients with benign prostatic hyperplasia (BPH) and the patients with advanced prostate cancer shown by a high degree of Gleason score (between seven and ten, page 32). In example 14, on page 30, the specification teaches that the patients with poorly differentiated advanced prostate cancers (high Gleason score) have no positive immunoreactivity of α inhibin in the tumor tissues (page 4, line 2). The result of the example is contrary to the response stated above "switch in function and expression of the inhibin molecule in advanced cancer", and the article of co-inventor Risbridger (figure 2), cited by the office in the previous office action, "the switch to an oncogenic state (metastatic state) is associated with an increase of inhibin levels". In addition, another article by same co-inventor, Risbridger et al., published in J of Urology (vol 171, page 192-196, 2004) teaches the patterns of expressing inhibin in the prostate cancer samples with different Gleason grades

and concludes that inhibin α is frequently overexpressed in high grade prostate cancer and also suggests that the role of inhibib α as a tumor suppressor needs to be reevaluated (abstract). Accordingly, both articles by co-inventor do contradict to the claimed invention and thus, one skilled in the art would not know how to practice the claimed method and would be forced into under experimentation for use a method of screening a mammal for prostate cancer by detecting the levels of inhibin. Therefore, the rejection is maintained for the reason of record.

***Conclusion***

NO claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Teni et al., (Clinical Chemistry, vol 35, page 1376-1379, 1989) disclose a method of screening for a mammal having prostate cancer comprising determining for the down-regulation of prostate inhibin-like protein. Teni et al., do not teach or suggest the method of detecting for down-regulation of inhibin protein or specific subunit, α-inhibin.

Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER